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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/565,417	08/03/2006	William J. Welsh	UMD0067US.NP	2667
46046	7590	05/05/2008	EXAMINER	
LICATA & TYRRELL P.C. 66 EAST MAIN STREET MARLTON, NJ 08053			SMITH, CAROLYN L	
ART UNIT		PAPER NUMBER		
1631				
NOTIFICATION DATE		DELIVERY MODE		
05/05/2008		ELECTRONIC		

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

poreilly@licataandtyrrell.com

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/565,417	WELSH ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Carolyn L. Smith	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

1) Responsive to communication(s) filed on 31 March 2008.

2a) This action is **FINAL**.                            2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

4) Claim(s) 1-4 is/are pending in the application.

4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.

5) Claim(s) \_\_\_\_\_ is/are allowed.

6) Claim(s) 1-4 is/are rejected.

7) Claim(s) \_\_\_\_\_ is/are objected to.

8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All    b) Some \* c) None of:

1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

1) Notice of References Cited (PTO-892)

2) Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_.

4) Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.

5) Notice of Informal Patent Application

6) Other: \_\_\_\_\_.

## **DETAILED ACTION**

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicants' submission, filed 3/31/08, has been entered.

Amended claim 1, filed 3/31/08, is acknowledged.

Claims herein under examination are 1-4.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Troyanskaya et al. (Bioinformatics, 2001, Volume 17, Number 6, pages 520-525) in view of Cunningham (US 2002/0129038 A1) with additional support from online Merriam-Webster dictionary (“Gaussian” definition).

Troyanskaya et al. describe methods for estimating missing values in DNA microarrays via imputing (abstract and title). Troyanskaya et al. describe k-means clustering and various model-based approaches and algorithms, such as (Single Value Decomposition) SVDimpute algorithm via normalization for microarray data comprising rows and columns (page 520, col. 2, first and second paragraphs; page 521, col. 1, first and second and fourth paragraphs and col. 2, first and last paragraph). According to the online Merriam-Webster dictionary, the definition of “Gaussian” is “being or having the shape of a normal curve or a normal distribution” (this definition is not being used as prior art, but rather to clarify the definition of the term “Gaussian”). The normalization of data represents normal distributions or Gaussian distributions or models. Troyanskaya et al. describe using k eigengenes, using a row average, and an expectation maximization method that is repeated until the change falls below a threshold (converges) (page 522, col. 1, third and fourth paragraphs). Troyanskaya et al. describe a website, software and methods implemented on a computer (abstract and page 524, col. 1, last paragraph) which represents a computer readable medium and program and computer which inherently contains memory and output of missing values. Troyanskaya et al. do not recite a model which imposes a mixture of multivariate normal distributions.

Cunningham describes a computer system and computer readable media with data storage devices as well as an expectation-maximization algorithm that is performed in a computer implemented data mining system to create a Gaussian Mixture Model as well as generating output describing clustering in the data by computing a mixture of multivariate normal distributions (abstract, 0015, 0028, 0030-0033, 0042).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the expectation-maximization method computing a mixture of multivariate normal distributions of Cunningham in the method of Troyanskaya et al. wherein the motivation would have been to employ a clustering algorithm that can work with large datasets and provide significant enhancements to a Gaussian Mixture Model, as stated by Cunningham (0015-0016, 0022) since there is a need to increase the range of data sets to which the algorithms can be applied, as stated by Troyanskaya et al. (abstract). One of ordinary skill in the art would have expected success since both Troyanskaya et al. and Cunningham use the expectation maximization method.

Thus, Troyanskaya et al. in view of Cunningham make obvious the invention.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1 and 3 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hytopoulos et al. (US 2002/0169560 A1) in view of Cunningham (US 2002/0129038 A1) with additional support from online Merriam-Webster dictionary (“Gaussian” definition).

Hytopoulos et al. describe a computer-implemented method and a system using microarray expression data arrays, cluster arrays, and clustering tools wherein the expression values have been normalized, filtered, and imputed, wherein missing data are imputed, and

outputted (abstract and paragraphs 0002, 0052, 0084, and 0123). According to the online Merriam-Webster dictionary, the definition of “Gaussian” is “being or having the shape of a normal curve or a normal distribution” (this definition is not being used as prior art, but rather to clarify the definition of the term “Gaussian”). The normalization of data represents normal distributions or Gaussian distributions or models. Hytopoulos et al. describe using a computer readable medium in association with a computer including a processor and memory and computer instructions which are configured to cause a computer to process data (claim 15) which represents an algorithm and computer software program and product. Hytopoulos et al. describe allowing the user to select K-nearest neighbor imputation mechanism or other data imputation mechanisms (paragraph 0125). Hytopoulos et al. describe analysis of gene expression data to form clusters (abstract). Hytopoulos et al. describe identifying genes represented in respective rows (paragraph 0038) which represents a partitioning of rows of microarray data. Hytopoulos et al. describe mapping rows of expression data (paragraph 0131). Hytopoulos et al. do not describe a model which imposes a mixture of multivariate normal distributions.

Cunningham describes a computer system and computer readable media with data storage devices as well as an expectation-maximization algorithm that is performed in a computer implemented data mining system to create a Gaussian Mixture Model as well as generating output describing clustering in the data by computing a mixture of multivariate normal distributions (abstract, 0015, 0028, 0030-0033, 0042).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the expectation-maximization method computing a mixture of multivariate normal distributions of Cunningham in the method of Hytopoulos et al. wherein the motivation

would have been to employ a clustering algorithm that can work with large datasets and provide significant enhancements to a Gaussian Mixture Model, as stated by Cunningham (0015-0016, 0022) since the amount of genetic data is quite large and an effective mechanism is needed to determine which genes are correlated with various human conditions, as stated by Hytopoulos et al. (0004 and 0009).

Thus, Hytopoulos et al. in view of Cunningham make obvious claims 1 and 3.

***Claim Rejections – 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. (e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hytopoulos et al. (US2002/0169560 A1) with additional support from online Merriam-Webster dictionary (“Gaussian” definition) in view of Cereghini et al. (US 6,496,834 B1).

Hytopoulos et al. describe the limitations in instant claims 1 and 3, as discussed above in the 35 USC 102 rejection. Hytopoulos et al. do not describe repeating a classification expectation-maximization algorithm until the K partitions converge or a model which imposes a mixture of multivariate normal distributions.

Cereghini et al. describe a method of performing cluster analysis inside a relational database management system using Gaussian mixture parameters and implementing an Expectation-Maximization (EM) clustering algorithm iteratively (abstract). Cereghini et al. describe grouping a set of data into k clusters with k rows (partitioned) (col. 2, lines 57-63). Cereghini et al. describe the expectation-maximization algorithm converges quickly and performing iterations (col. 9, lines 34-42). Cereghini et al. describe the EM algorithm assumes the data is formed by the mixture of multivariate normal distributions.

Hytopoulos et al. state that effective mechanisms for analyzing DNA array data are needed to determine which genes or combination of genes are correlated to various human conditions (paragraph 0009). Cereghini et al. state the EM algorithm is robust for noisy data and missing information (col. 7, lines 5-6). Cereghini et al. state cluster analysis does not typically work well with large databases due to memory limitations and the execution times required (col. 2, lines 32-39). It would have been obvious to one of ordinary skill in the art at the time the invention was made to use effective means for analyzing DNA array data, as stated by Hytopoulos et al., by using algorithms supporting large databases, as stated by Cereghini et al.

The person of ordinary skill in the art would have been motivated to make that modification in order to find effective ways (as stated by Hytopoulos et al. and Cereghini et al.) of correlating genes to human conditions (as stated by Hytopoulos et al.) by allowing non-statisticians to benefit from advanced mathematical techniques available in a relational environment, as stated by Cereghini et al. (col. 2, lines 40-43).

Thus, Hytopoulos et al. with additional support from the online Merriam-Webster dictionary, in view of Cereghini et al. make obvious the instant invention.

Applicant argues instant claim 1 has been amended to indicate the Gaussian mixture clustering model imposes a mixture of multivariate normal distributions. It is noted that at least one of the prior art references in each of the 35 USC 103 rejections above recite this limitation.

***Other prior art made of record***

Although not being used as prior art, Yeung et al.'s "Model-based clustering and data transformations for gene expression data" (Bioinformatics, 2001, Volume 17, Number 10, pages 977-987) is being put on the record. Yeung et al. discuss Gaussian mixture models for clustering in gene expression data analysis and the ability to incorporate missing data into the model.

***Conclusion***

No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center. The faxing of such papers must conform to the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR §1.6(d)). The Central Fax Center number for official correspondence is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carolyn Smith, whose telephone number is (571) 272-0721. The examiner can normally be reached Monday through Thursday from 8 A.M. to 6:30 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran, can be reached on (571) 272-0720.

April 29, 2008

/Carolyn Smith/  
Primary Examiner  
AU 1631